Increased costs of prescribing are likely to be a further consequence of contact with representatives. Selective serotonin reuptake inhibitors are just one example where promotion by drug companies has boosted sales far beyond levels that might have been expected if non-promotional literature had been heeded. Despite a widely available and authoritative review counselling caution in their use[7]—a policy subsequently born out by later evidence[8]—sales of selective serotonin reuptake inhibitors soared, with consequent increases in spending. As has been pointed out before,[9] these resources could perhaps have been better used elsewhere. Given the Byzantine nature of drug pricing in the NHS, it is a matter of speculation what effect there might be on drug expenditure nationally if we all stopped seeing representatives, but at local level it would be surprising if such a move did not bring real benefits.

Changing our habits may not necessarily be easy. Many drug company representatives are delightful and estimable individuals. They are friendly, helpful people who treat doctors with respect and value their time—not a reception doctors get from every quarter. Doctors in turn may feel a sense of obligation and may see representatives as a matter of courtesy. Can we really afford to do this? A particular group targeted by pharmaceutical companies are junior doctors—the prescribers of tomorrow. We should consider how this problem might be managed in hospitals and in general practice training by devising ways of educating new doctors about the pitfalls they may encounter in seeing representatives.

There is potentially much to be gained by changing our ways. We could cut costs, improve our prescribing practices—and save a little time in our crowded schedules. With more new and expensive drugs now hitting the market, this might be an ideal time for change.

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BMJ competing interest: The *BMJ* might possibly benefit financially if doctors were to see fewer drug company representatives because resources saved might be spent on advertising.

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Prescribing medicines for children

Major problems exist, but there are some promising developments

All parents would like the drugs administered to their child to have been fully evaluated using studies based in children (but not their child). However, infants and older children present a challenge for drug monitoring and testing, and there are far fewer clinical studies designed to test drugs in children than to test them in adults. The factors that limit such studies include technical constraints such as blood sampling. There are also ethical difficulties in involving children in studies that may not directly benefit them, even if the studies involve minimal risk. Fortunately, with the development of new non-invasive methods to measure drug concentrations therapeutic drug monitoring will be less limited by the necessity for blood sampling.[1] Moreover, drug regulatory authorities and professional bodies are beginning to address the need to test drugs for children in the same way as those for adults.

The disposition of drugs in children varies from that in adults because children differ from adults pharmacokinetically and pharmacodynamically. Factors such as growth, surface area, organogenesis, enzyme development, plasma and tissue binding, brain development, physiological and functional development, and psychosocial issues need to inform the development of new medicines in children. Unsurprisingly, adverse drug reactions are also different. The so called "grey baby syndrome" with chloramphenicol[2] might have been avoided with adequate knowledge of routes of metabolism and immature physiology, but other such deaths associated with propofol[3] remain poorly understood.

Many drugs given to children in the United Kingdom are unlicensed or prescribed "off label." The so called off label prescribing of a licensed medication to a patient outside the specification of the product licence involves medicines being administered by an unlicensed route, in an unlicensed formulation or dosage, or to a child below the stated age range. Yet without such prescribing effective treatment would be denied to many children. A recent British study found that one third of all patients admitted to a general paediatric medical or surgical ward received one or more unlicensed or off label drug during their stay.[4] In the United States nearly 80% of the new drugs approved in 1984-9 had no indication for use in children.[5] Some medicines given to children are not licensed for human administration at all. These so called "orphan drugs"—such as sodium benzoate, caffeine, tolazoline—are not licensed by their manufacturers because the cost involved in obtaining a licence may never be recovered.

Drug errors are a further important problem. Recent concerns about the deaths of babies who were

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given miscalculated doses of common drugs (morphine, digoxin) is reflected by reports in the medical literature suggesting an increase in drug errors.[6] Most paediatricians have at least second hand experience of incidents in which a child's care has been compromised by medication errors. The difficulties of using medicines formulated in adult dose volumes are often compounded by complex dilutions and rate calculations (such as µmol/kg/min) being performed by tired medical staff.[7] Medication errors could be reduced by the use of software programmes such as those in use in general practice,[8] but such systems are seldom evident on paediatric wards. Reports emphasise the need for a systematic approach to avoid such events, including close attention to prescription writing, pharmacy dispensing, and nursing processes.[9]

In an attempt to improve this situation the European Agency for the Evaluation of Medicinal Products has given guidance to pharmaceutical companies on the need to conduct clinical trials in children. This states that there is a shared responsibility to ensure that children are not denied timely access to safe and effective medicines which have accurate, scientifically justified prescribing information.

In a more robust directive the Food and Drug Administration in the United States has declared that new drugs likely to be used to treat children must be tested by pharmaceutical companies for their effects in children.[10] Existing drugs used off label may also be required to have their licences amended if there is substantial use in childhood.[10] The National Institutes of Health have established a paediatric pharmacology unit, based in seven centres, which provides a base for clinical trial coordination by paediatric pharmacologists. A similar centre should be developed in the European Union. To encourage the development of orphan drugs, the Australian Therapeutic Goods Administration has waived its evaluation fee for orphan drugs. Orphan drug legislation in Europe is awaited.

In the United Kingdom the Royal College of Paediatrics and Child Health has produced a formulary, *Medicines for Children*, published last week. This formulary is divided into three sections: a therapeutics section, a drug monograph section (with information on licensed, unlicensed, and off label use of drugs), and a dietary section on borderline substances. The secondary aims of this initiative are to establish a database on the efficacy and safety of medicines given to children that can be used by those who make, test, market, prescribe, dispense, and administer medicines for children. A nation's children are its investment in the future. There must be further progress in the development and prescribing of medicines for children to ensure that children do not remain therapeutic orphans.[11]

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Skin and nail fungi—almost beaten

Don't get confused by the "evidence"

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Dermatophyte infections occur often either between the outer toes or in the toenails. It is now possible to eradicate most of these, and more widespread fungal infections, with the new generation of antifungal agents. Competing claims are made for systemic terbinafine and itraconazole, and up to now it has been hard to sort out the science from the marketing. The recent paper by Evans et al[1] and the systematic review in this issue by Hart et al (p 79)[2] attempt to point ways through the evidence. Other problems remain in treating children and non-responders.

The conclusions reached in the systematic review by Hart et al are undermined by the limited questions asked. It is legitimate to review the evidence for topical treatments for superficial fungal infections of the skin, but common sense must be applied to the results. Use of topical drugs in the community is not necessarily the same as in a trial situation. Poor compliance is common because symptoms are rapidly relieved, whether or not there has been mycological cure. Very few applications of topical (fungicidal) terbinafine are needed to produce a cure, whereas fungistatic drugs must be applied until the infected stratum corneum is shed. One week of topical terbinafine therefore gives better cure rates than four weeks of clotrimazole.[3] The implications for community cure rates, recurrence, and spreading of infection to others are obvious and the authors' failure to consider them indicate a naivety in their cost effectiveness conclusions.

Moreover, in considering nail infections it is inappropriate to review the evidence for topical treatment in isolation from that for systemic treatment. In their discussion Hart et al correctly state that evidence on the efficacy of topical treatments for nail infections is sparse, but the summary conclusion ambiguously implies that their conclusions apply to nail as well as the skin.[2] Systemic therapy, with terbinafine, is the treatment of choice for onychomycosis.[1]

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